IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 3, Issue 1, January 2023
Impact Factor: 7.301

Review on Current Good Manufacturing Practice

J. B. Salgar, S. K. Bais, Pranali S. Sawant
Fabtech College of Pharmacy, Sangola, Solapur, Maharashtra, India

Abstract: *Good Manufacturing Practices (GMP) is procedures that must be followed in order to adhere to the recommendations made by the organisations in charge of authorising and regulating the manufacture and sale of pharmaceutical products. With the use of these rules, manufacturers can ensure that their goods are consistently of a high quality for the intended use from batch to batch. Cosmetics, nutritional supplements, food and beverages, and medical equipment are all subject to the GMP. However, the main goal of GMP is always to prevent harm from occurring to the end user. This includes making sure that the final product is free from contamination that its manufacture is consistent, and that it has been thoroughly documented. The staffs are well-trained, and the product has through more than just the last round of quality inspection. Typically, a quality management system is used effectively to assure GMP. To control pharmaceutical production and packaging processes, the term GMP was first used. The guide to GMP, commonly known as the Orange Guide, was created by the Medicine Inspector of the Department of Health and Social Security of England in cooperation with other concerned parties. The 1977 publication of the second version (52 pages, five appendices). In 1983, the third version (110 pages, 5 appendices) was released.*

Keywords: Good Manufacturing Practices

I. INTRODUCTION

- Good Manufacturing Practices (GMP) are procedures that must be followed in order to adhere to the recommendations made by the organisations in charge of authorising and regulating the manufacture and sale of pharmaceutical products. With the use of these rules, manufacturers can ensure that their goods are consistently of a high quality for the intended use from batch to batch. Cosmetics, nutritional supplements, food and beverages, and medical equipment are all subject to the GMP. However, the main goal of GMP is always to prevent harm from occurring to the end user. This includes making sure that the final product is free from contamination that its manufacture is consistent, and that it has been thoroughly documented. The staff is well-trained, and the product has through more than just the last round of quality inspection. Typically, a quality management system is used effectively to assure GMP.
- To control pharmaceutical production and packaging processes, the term GMP was first used. The guide to GMP, commonly known as the Orange Guide, was created by the Medicine Inspector of the Department of Health and Social Security of England in cooperation with other concerned parties.
- The 1977 publication of the second version (52 pages, five appendices). In 1983, the third version (110 pages, 5 appendices) was released.

1.1 CGMP

- CGMP refers to Current Good Manufacturing Practices Regulation enforced by the FDA
- Provide for system that assure proper design, monitoring, and control of manufacturing processes and facilities
- CGMP is applicable to the pharmaceutical, biotechnology, medical technology, and medical device industries, ensuring the identification, strength, quality, and purity of drug items being made.
- The goal of CGMP is to increase quality of the product.
- The Manufacturers of Medicines have adequate control over manufacturing operations, which involves the establishment of strong quality management systems, sourcing quality raw materials, operating procedures, detecting and investigating deviation in product quality, and trustworthy testing laboratories.
- If properly implemented, CGMP reduces the likelihood of product contamination, mixups, deviations, failures, and errors, ensuring that drug products satisfy the necessary quality requirements.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 3, Issue 1, January 2023
Impact Factor: 7.301

- The procedure for approving a marketing application for a new generic medicine includes an assessment of the manufacturing process to ensure that it complies with CGMPS assessors and investigators from the FDA decide if the company has the facilities, tools, and capacity to produce the
- Medication it proposes to market.
- CGMP is crucial because consumers lack the means to determine whether the medication they are taking is safe and effective because testing alone cannot guarantee product quality.
- To ensure that quality is included into the design and manufacturing process at every stage, it is crucial that drugs be made in accordance with the conditions and procedures mandated by the CGMP rules; Facilities in good shape, equipment that is regularly serviced and calibrated, personnel who have the necessary qualifications and training, and procedures that are dependable and repeatable

1.2 Guideline

- To keep manufacturing facilities sanitary and clean.
- To keep the environment under strict control in order to avoid cross-contamination that could make the product unfit for human consumption.
- Manufacturing procedures must be precisely controlled and defined. Every essential procedure is frequently validated to guarantee consistency and adherence to the necessary requirements.
- Any changes that might have an impact on the drug's quality are confirmed.
- Following best practises for documentation.
- Consistent instruction of operators in document procedures.
- Keeping records—either manually or digitally—during the manufacturing process to show that all the processes necessary to follow the instructions and procedures were carried out, and that the drug's consistency in both quantity and quality.
- Any discovered deviations must be looked into and recorded.
- Manufacturing and distribution records that allow for the full history of a batch to be tracked, stored, and retrieved.
- Distribution of goods must reduce any threat to their calibre.
- A recall system must be in place in order to remove any batch from distribution or sale.
- It is important to evaluate complaints regarding marketed items, identify the root causes of quality flaws, and take appropriate action to fix the problem and stop it from happening again.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 3, Issue 1, January 2023
Impact Factor: 7.301

1.3 Objective

- Ensure that products are regularly produced and held to the required quality standards.
- Interested in every element of production and quality assurance
- General oversight and supervision of cosmetic product manufacturing.
- Make certain the consumer obtains a product of the desired calibre.
- The starting materials, production and quality control procedures, buildings, equipment, and staff involved all affect the product's quality.

II. DIFFERENCE BETWEEN CGMP AND GMP

GMP	CGMP
Optimum manufacturing procedures it is a GMP Even without Validation.	Optimum manufacturing procedures when validated, it becomes a CGMP.
Over 100 nations follow the good manufacturing practices (GMP) set of guidelines.	CGMP stands for Current good manufacturing practises, which member nations must follow.
GMP is used with pharmaceutical and healthcare items, Helping to uphold their high standards.	CGMP serves as a Reminder to accepting nations that all regulations must be adhered to using the most recent and up-to-date production techniques.

III. CODE OF FEDERAL REGULATIONS

The FDA's section of the CFR is included in Title 21, which interprets the Public Health Service Act and related acts as well as the Federal Food, Drug, and Cosmetic Act. Parts 1-99, 200-299, 300-499, 600-799, and 800-1299 of Title 21 contain regulations pertaining to pharmaceutical or medication quality.

The regulations provide a shared understanding of the regulatory procedure by outlining the standards that drug producers, applicants, and FDA must adhere to.

- **21 CFR PART 314:** To obtain FDA permission before marketing a new medicine.
- **21 CFR PART 210 :** The General Part of Current Good Manufacturing Practice in the Manufacturing, Processing, Packing, or Holding of Drugs. This regulates cGMP for the production, processing, packaging, or storage of pharmaceuticals. The definitions for terminology used in the regulations, such as batch, lot, etc., are included in Part 210.
- **21 CFR PART 211:**Finished pharmaceuticals current good manufacturing practises. Finished pharmaceuticals are those. For instance, Part 210 would apply to a liquid medication that leaches through a plastic container, whereas Part 211 would probably apply to a tablet that separates after shipping.
- **21 CFR PARTS 212:** Currently Accepted Good Manufacturing Practice for Drugs for Positron Emission Tomography.
- **21 CFR PARTS 600:** General Biological Products. Important terminology, establishment standards, establishment inspection requirements, and adverse experience reporting requirements are included in this document that relates to biological products.
- **21CFRPART11:** Electronic Signatures; Electronic Records. The policies regarding electronic records and electronic signatures are contained here. The standards for determining whether electronic documents and electronic signatures meet the same standards as paper records in Part 11 are laid out. Electronic filings to the FDA are likewise covered by Part 11.

Current Good Manufacturing Practice (CGMP) training is required for all employees who work in the production, packaging, storage, distribution, or transportation of medicines and other medical items.

CGMPs in finished pharmaceutical Manufacturing

- 21 CFR Parts 210 & 211 are applicable to pharmaceutical manufacturing
- 21 CFR Part 210: current good Manufacturing practices in manufacturing, processing, Packing, or Holding of Drugs; General

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 3, Issue 1, January 2023
Impact Factor: 7.301

210.1 Status of Current Good Manufacturing Practice Regulations.

(a) The guidelines outlined in this part, along with parts 211 (Current Good Manufacturing Practice For Finished Pharmaceuticals), 225 (Current Good Manufacturing Practice For Medicated Feeds), and 226 (Current Good Manufacturing Practice For Type A Medicated Articles) of this chapter, contain the minimal current good manufacturing practise for the methods to be used in, and the facilities or controls to be used for, the manufacture, processing, packing, or holding of a drug to address the concerns of the FDA.

210.2 Applicability of current good manufacturing practice regulations.

210.3 Definitions.

CGMPs in Pharmaceutical Manufacturing

- **21 CFR Parts 210 & 211 are applicable to pharmaceutical manufacturing**
- **21 CFR Part 211: Current Good Manufacturing**

IV. FINISHED PHARMACEUTICALS

- **Subpart A –** General Provisions: For prescription drugs, biologics, and OTC drugs
- **Subpart B –** Organization and Personnel: Quality control unit, personnel responsibilities
- **Subpart C –** Buildings and Facilities: Design & construction, lighting, HVAC, plumbing
- **Subpart D – Equipment:** Design & construction, cleaning, maintenance, automation
- **Subpart E –** Control of Components and Drug Product Containers and Closures – Receipt and storage of components, component testing, use and rejection
- **Subpart F –** Production and Process Controls: Written procedures, deviations, Eq. ID's
- **Subpart G –** Packaging and Labelling Control: Examination, labelling, inspection, dating
- **Subpart H –** Holding and Distribution: Warehouse and distribution procedures
- **Subpart I –** Laboratory Controls: Test and release for distribution, stability, and contamination
- **Subpart J –** Records and Reports: Equipment cleaning log, production records, and complaints.

210.1 Status of Current Good Manufacturing Practices Regulations:

The regulations outlined in this part and in parts 211, 225, and 226 of this chapter contain the minimum current good manufacturing practises for methods to be used in, and the facilities or controls to be used for, the manufacture, processing, packing, or holding of a drug in order to ensure that such drug complies with the act's requirements with regard to safety, and has the identity and strength, as well as the quality and purity characteristics that it is purported to possess.

The regulations outlined in this part and in parts 211, 225, and 226 of this chapter contain the minimum current good manufacturing practises for methods to be used in, and the facilities or controls to be used for, the manufacture, processing, packing, or holding of a drug in order to ensure that such drug complies with the act's requirements with regard to safety, and has the identity and strength, as well as the quality and purity characteristics that it is purported to possess.

210.2 Applicability Of Current Good Manufacturing PracticeRegulations:

The rules in this section, parts 211, 225, and 226 of this chapter as they may apply to drugs, parts 600 through 680 of this chapter as they may apply to biological products for human use, and part 1271 of this chapter as they may apply to human cells, tissues, or cellular or tissue-based products (HCT/P) that are drugs (subject to review under an application submitted under section 505 of the act or under a biological product licence application).Unless the rules specifically state otherwise, the regulation that is directly applicable to the drug product in issue shall prevail in the case of a disagreement between applicable regulations in this part and other parts of this chapter. When applicable laws from this part and other sections of this chapter conflict, the regulation that is more precisely applicable to the drug product in question shall take precedence.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 3, Issue 1, January 2023
Impact Factor: 7.301

210.3 Definition:

When terms are used in this part and parts 211, 225, and 226 of this chapter, they must be interpreted in accordance with section 201 of the act

This section, as well as parts 211, 225, and 226 of this chapter, all uses the definitions below.

1. **Act** which refers to the Federal Food, Drug, and Cosmetic Act as amended (21 U.S.C. 301 et seq.).
2. **Batch** indicates a precise quantity of a medication or other substance that is manufactured in accordance with a single manufacturing order and is created throughout the same manufacturing cycle, with the goal of having uniform character and quality, within certain bounds.
3. **Component** implies any substance used in the production of a drug product, even if it doesn't end up in the final product.
4. **Drug** The term "product" refers to a completed dosage form, such as a pill, capsule, solution, etc., that typically, but not always, also contains inactive components. The phrase also refers to a final dose form meant to serve as a placebo but devoid of any active ingredients.
5. **Fiber** implies any contaminating particle that is at least three times longer than it is wide.
6. **Nonfiber** Any filter that, following the proper pre-treatment, such as washing or flushing, will not release fibres into the component or drug product that is being filtered is referred to as a releasing filter.
7. **Active Ingredient** means any element that has the potential to have pharmacological effects or other direct effects on the structure or any function of an animal or human body, or on the diagnosis, mitigation, treatment, or prevention of disease. The term includes any elements that might go through chemical transformation during drug product manufacturing and exist in the drug product in a modified form designed to provide the desired activity or effect.
8. **Inactive Ingredients** refers to any element that is not an active substance.
9. **In-process Material** implies any substance created, mixed, compounded, or manufactured through a chemical reaction and used to prepare the drug product.
10. **Lot** means a batch or a specific identified portion of a batch that has uniform character and quality within certain limits; or, in the case of a drug product made using a continuous process, it means a specific identified amount produced in a unit of time or quantity in a way that ensures its having uniform character and quality within certain limits.
11. **Lot Number, Control Number, Or Batch Number**denotes any unique set of letters, numbers, or symbols, or any combination of them, that can be used to trace the production, processing, packaging, storage, and distribution of a batch or lot of a medicine product or other item.
12. **Manufacturing, Processing, packing, or holding of a drug product***Including*activities related to drug product testing, labelling, and packaging.
13. **Quality control unit** denotes any individual or organisational component chosen by the company to carry out the tasks related to quality control.
14. **Strength means** The potency, which is the therapeutic activity of the drug product as evidenced by proper laboratory tests or by sufficiently generated and controlled clinical data, and/or The concentration of the drug substance (for example, weight/weight, weight/volume, or unit dose/volume basis) (expressed, for example, in terms of units by reference to a standard).
15. **Theoretical yield** signifies the amount that, depending on the number of components to be used, would be produced at any suitable stage of manufacture, processing, or packing of a certain drug product, if there were no loss or error in actual production.
16. **Actual yield** signifies the amount that is really created at any suitable stage of the manufacture, processing, or packaging of a specific drug product.
17. **Percentage of theoretical yield** indicates, expressed as a percentage, the relationship between the actual yield (at any suitable phase of manufacture, processing, or packing of a certain drug product) and the clinical theoretical yield (at the same phase).

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 3, Issue 1, January 2023
Impact Factor: 7.301

18. **Acceptance criteria** implies the requirements for deciding whether to accept or reject a lot or batch, including the product standards and acceptance/rejection criteria, such as acceptable quality level and unacceptable quality level, with a corresponding sampling plan (or any other convenient subgroups of manufactured units).
19. **Representative sample** means a sample made up of several units drawn according to logical criteria, such as random sampling, with the goal of ensuring that the sample accurately represents the material being sampled.
20. **Gang-printed labelling** implies labelling made from a sheet of material that has multiple labelling items printed on it.

CFR Part 211: Current Good Manufacturing Subpart A – General Provision

(a) Scope

For the preparation of drug products (excluding positron emission tomography drugs) for administration to humans or animals, the regulations in this part contain the minimum current good manufacturing practise.

Subpart B Organization and personnel:-

211.22 Responsibility of Quality Control Unit

A quality control unit must be established, and it must have the power to approve or reject all parts, drug product containers, closures, in-process materials, packaging materials, labelling, and drug products. It must also have the power to examine production records to ensure that no mistakes were made, or that mistakes that had been made had been thoroughly investigated. The task of approving or rejecting drug items made, processed, packed, or kept under contract by another business falls to the quality control unit.

The quality control unit shall have access to adequate laboratory facilities for the testing and approval (or rejection) of components, drug product containers, closures, packaging materials, in-process materials, and drug products.

The task of approving or rejecting any specifications or processes that have an impact on the identity, strength, quality, and purity of the drug product falls to the quality control unit.

211.25 Personnel Qualifications

Each person involved in the production, processing, packaging, or storage of a drug product must possess the necessary education, training, and experience—or any combination of these—to carry out the tasks that have been delegated to them. Training must cover both the specific activities that the employee conducts as well as current good manufacturing practise as it relates to those operations (including this chapter's regulations on current good manufacturing practise and the documented procedures that these regulations require). Employees must get ongoing training in current good manufacturing practise from certified personnel frequently enough to ensure that they are aware with the rules that apply to them.

211.28 Personnel Responsibility

- All employees who work on the production, processing, packaging, or storage of pharmaceutical products are required to wear clean clothes that are suitable for their jobs. It is required to wear protective clothing, such as head, face, hand, and arm coverings, to prevent contamination of drug goods.
- The staff must follow hygienic and healthy practises.
- The areas of the buildings and facilities designated as limited-access areas may only be accessed by staff members who have been authorised by supervisory staff.

Subpart c – Building and Facilities

211.42 Design and Construction Features

Any facility or buildings used in the production, processing, packing, or storage of a pharmaceutical product must be of an appropriate size, design, and location to allow for easy upkeep, maintenance, and efficient operations.

Operations must be carried out in clearly defined spaces that are big enough. To prevent contamination or mix-ups during the following procedures, there must be distinct, clearly defined locations or other control mechanisms for the firm's operations:

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 3, Issue 1, January 2023
Impact Factor: 7.301

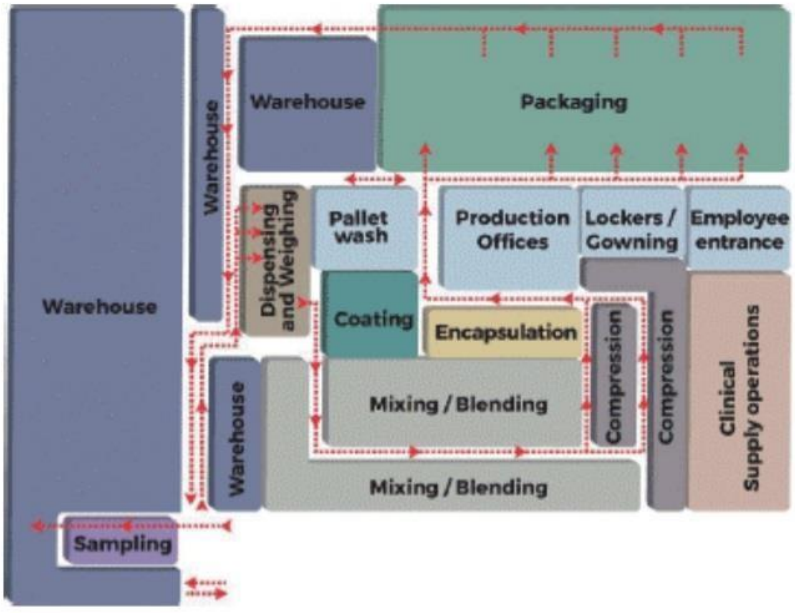
components, drug product containers, closures, and labelling must be received, identified, stored, and held back from use until the necessary sampling, testing, or examination by the quality control unit has been completed before being released for manufacture or packing;
Preserving the containers, closures, and labelling of drug product components that have been rejected before disposal;
Containers, closures, and labelling for drug products, as well as the storage of released components;
Keeping finished items in storage
Operations including production and processing;
Packaging and labelling operations;
Quarantine storage prior to medication product release;
After release, drug product storage;
Controlling and running the lab;
As appropriate, aseptic processing also includes:
Smooth, firm, and readily cleanable surfaces for the floors, walls, and ceilings;
Controls for humidity and temperature;
A positive-pressured air supply that is filtered by high-efficiency particulate air filters, whether or not the flow is laminar; (iv) a system for monitoring environmental conditions;
A system for maintaining any equipment used to manage the aseptic conditions;
A system for cleaning and disinfecting the space and the equipment to create aseptic conditions.
Penicillin manufacturing, processing, and packaging tasks must be carried out in facilities apart from those used for other drugs intended for human consumption.

Layout:

- Planned and organised arrangements between and among departments
- Proper layout helps in: Increases productivity aids in efficient use of people, resources, money, and equipment

Type of layout :

- Circular flow
- Parallel flow
- Cross over traffic



IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 3, Issue 1, January 2023
Impact Factor: 7.301

211.44 Lighting

All spaces must have sufficient illumination

211.46 Ventilation, air filtration, air heating and cooling:

When necessary for the manufacture, processing, packing, or holding of a drug product, equipment for proper control over air pressure, microorganisms, dust, humidity, and temperature shall be provided.

An air supply that has been positively pressed through high-efficiency particulate air filters, whether or not the flow is laminar or nonlaminar.

Proper ventilation must be offered.

211.48 Plumbing

In order to avoid contaminating any drug product, potable water must be supplied under constant positive pressure in a plumbing system that is free of flaws.

Drains must be large enough and equipped with an air break or other mechanical device to prevent back-siphonage when connected to a sewer directly.

211.50 Sewage and Refuse

The building and nearby property's sewage, trash, and other refuse must be removed and disposed of in a safe and sanitary way.

Sufficient washing facilities must be available, including easy access to clean restrooms, hot and cold running water, soap or detergent, air dryers, and single-use towels.

211.52 Washing and toilet facilities:

Adequate washing facilities must be offered, including easy access to clean restrooms, hot and cold running water, soap or detergent, air dryers, and single use towels.

Subpart D – Equipment

211.63 Equipment design size, and location:

•The equipment used in the production, processing, packing, or storage of a drug product must be of the right design, size, and location to make it easy to operate it for its intended purpose as well as for cleaning and maintenance.

211.65 Equipment construction

- Equipment must be built so that surfaces that come into contact with parts, materials used during production, or drug products are not reactive, additive, or absorbent in ways that go beyond what is required by law or other recognised standards.
- In order to prevent the components, drug product containers, closures, in-process materials, or drug products from being altered beyond the official or other defined requirements, any operating-related fluids, such as lubricants or coolants, must not come into touch with them.

211.67 Equipment cleaning and maintenance

Equipment and utensils shall be cleaned, maintained, and, as appropriate for the nature of the drug, sanitized and/or sterilized at appropriate intervals to prevent malfunctions or contamination that would alter the safety, identity, strength, quality, or purity of the drug product beyond the official or other established requirements.

Written protocols must be established and followed for the upkeep of tools used in the production, processing, packing, or storage of drug products, including cutlery.

These procedures must include the following, but are not required to:

Responsibility for equipment upkeep and cleaning assigned;

Schedules for maintenance and cleaning, including, where necessary, sanitising regimens;

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 3, Issue 1, January 2023
Impact Factor: 7.301

A thorough explanation of the procedures, tools, and supplies utilised in cleaning and maintenance work, as well as how to properly disassemble and reassemble equipment as required to ensure proper cleaning and maintenance;
Protection of clean equipment from contamination prior to use
Removal or erasure of previous batch identification
Quick inspection of the equipment's cleanliness are all required.

211.72 Filters

- Liquid filtration filters that are used in the production, processing, or packaging of injectable medication products intended for human use must not release fibres into such products. When it is impossible to produce such items without the usage of these filters, fiber-releasing filters may be utilised.
- Create these things without utilising these filters. In order to lower the amount of particles in the injectable drug product, a second nonfiber-releasing filter with a maximum nominal pore size rating of 0.2 micron (0.45 micron if the production conditions so require) must be employed if the use of a fiber-releasing filter is required. An asbestos-containing filter cannot be used.

Subpart E – Control of component and drug product container and closures:

211.80 General provision

- The receipt, identification, storage, handling, sampling, testing, and approval or rejection of components and drug product containers and closures must all be described in written procedures that are followed.
- Always handle and store components, drug product containers, and closures in a way that prevents contamination.
- For components, drug product containers, or closures, each container or collection of containers must be marked with a distinctive code for each lot in each shipment received. Each lot's disposition will be recorded using this code. Each lot must be properly labelled with its status (i.e., quarantined, approved, or rejected).

211.82 Receiving and storing untested parts, containers, and closures for drugproducts.

- Each container or collection of containers for components, drug product containers, and closures must be visually inspected upon receipt and prior to acceptance to ensure proper labelling of contents, absence of damage or broken seals, and contamination.
- Components, drug product containers, and closures must be quarantined until they have undergone testing or examination, as necessary, and have been released. Storage inside the region must comply with 211.80's standards.

211.84 Medicinal product containers, closures, and component testing and approvalor rejection.

The quality control unit must sample, test, or otherwise thoroughly analyse each lot of components, drug product containers, and closures before approving it for use.
The following steps must be followed for collecting samples:

- To collect samples, the following procedures must be followed:
- The containers must be opened, sampled, and resealed in a way that guards against contaminating both their contents and other parts, the containers for drug products, or the closures.
- When necessary, sterile tools and aseptic sampling methods must be employed.
- Such sample subdivisions shall not be composited for testing if a component must be sampled from the top, middle, and bottom of its container.
- The name of the material sampled, the lot number, the container from which the sample was obtained, the date the sample was taken, and the identity of the person who collected the sample must all be clearly visible on sample containers.
- Sample-taking containers must be marked to indicate that samples have been taken from them.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 3, Issue 1, January 2023
Impact Factor: 7.301

211.86Use of components, drug product containers, and closures that have beenapproved

Rotate the permitted components, drug product containers, and closures so that the oldest approved stock is used first. This condition may be disregarded if the departure is reasonable and only temporary.

211.87 medicinal product containers, closures, and permitted parts undergoing newtesting.

Components, drug product containers, and closures must be retested or reexamined, as necessary, for identity, strength, quality, and purity. The quality control unit must then decide whether to accept or reject the component, drug product container, or closure in accordance with 211.84, for example, after prolonged storage or after exposure to air, heat, or other conditions that could harm them.

211.94 Drug product containers and closures:

- The safety, identity, strength, quality, or purity of the drug cannot be altered beyond what is required by law or regulation by the drug product's containers and closures.
- Systems for sealing containers must offer sufficient defence against foreseeable external variables during use and storage that could damage or contaminate the medication substance.
- To ensure that they are fit for their intended use, drug product containers and closures must be free of contaminants, sterilised where necessary based on the nature of the medicine, and processed to remove pyrogenic qualities. Validation of such depyrogenation techniques is required.
- For drug product containers and closures, standards or specifications, testing procedures, and, where applicable, cleaning, sterilising, and processing techniques to remove pyrogenic qualities, must all be documented and followed

Subpart F – Production and process control:

211.100 written procedure deviations:

(a)To ensure that the drug products have the identity, strength, quality, and purity that they claim or are represented to have, there must be established protocols for manufacture and process control. All requirements outlined in this subpart must be included in such processes. The appropriate organisational units must write, review, and approve these written procedures, as well as any revisions, before they are reviewed and authorised by the quality control unit.

211.105 Equipment identification:

- To accurately identify their contents and, if necessary, the batch's processing stage, all compounding and storage containers, processing lines, and large equipment utilised during the creation of a batch of a drug product must be displayed at all times.
- To identify the precise equipment used in the creation of each batch of a pharmacological product, major equipment must be identified by a distinctive identification number or code that must be entered in the batch production record. A distinctive identification number or code may be used in place of the name of the equipment in situations where a manufacturing facility only has one instance of a specific piece of equipment.

211.110 Sampling and testing of in process material and drug product:

Written procedures that specify the in-process checks, tests, or inspections to be carried out on suitable samples of in-process materials of each batch must be established and followed in order to ensure batch consistency and integrity of drug products. These control methods must be put in place in order to keep track of the results and verify the effectiveness of the manufacturing steps that may be to blame for variations in the properties of raw materials and finished pharmaceutical products. When necessary, these control measures must include, but are not limited to, the following:

Weight fluctuation of tablets or capsules

Time of disintegration

Sufficient mixing to ensure consistency and homogeneity;

The speed and duration of dissolution

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 3, Issue 1, January 2023
Impact Factor: 7.301

The clarity, completeness, or pH of the solution.
Testing for bioburden.

211.111 Time limitation on production:

- To ensure the quality of the drug product, time restrictions for completing each stage of production shall be defined as necessary. If the quality of the drug product is not compromised, deviating from stated time restrictions may be permissible. Such a divergence must be explained and supported by evidence.

211.112 Control of microbiological contamination:

It is necessary to adopt and adhere to appropriate documented procedures that are intended to prevent the growth of undesirable microorganisms in drug items that are not required to be sterile.
It is required to adopt and adhere to appropriate documented processes that are intended to avoid microbiological contamination of drug items that claim to be sterile. All aseptic and sterilisation processes must be validated as part of these procedures.

211.115 Reprocessing:

A system for reprocessing batches that don't meet standards or specifications must be established, and written procedures must be followed to specify the measures to be done to ensure that the reprocessed batches will meet all defined standards, specifications, and characteristics.
Reprocessing must be done with the quality control unit's assessment and approval.

Subpart G – Packaging and labelling control:

211.122 Material examination and usage criteria:

- Written procedures outlining the receipt, identification, storage, handling, sampling, examination, and/or testing of labelling and packaging materials must be followed because they provide sufficient detail. Before being used to package or label a drug product, labelling and packaging materials must be representatively sampled, examined, or tested upon receipt.
- Any labelling or packaging that complies with the necessary written requirements may be approved and made available for usage. Any packaging or labelling materials that fall short of these requirements must be rejected in order to keep them from being used in operations for which they are inappropriate.
- Records must be kept for every shipment of every type of labelling and packing material that is received, detailing receipt, examination or testing, and whether the shipment was accepted or denied.
- Labels and other labelling materials must be preserved individually and properly identified for each unique drug product, strength, dosage form, and quantity of contents. Only authorised workers are allowed access to the storage facility.

211.125 labelling issuance

- Labels distributed for use in drug product labelling processes must be strictly regulated.
- Labeling supplies that are distributed for a batch must be thoroughly inspected to ensure that they are genuine and match the labelling requirements indicated in the master or batch production records.
- All extra labels with lot or control numbers need to be disposed of.
- Returned labels must be maintained and stored in a way that ensures appropriate identification and prevents mix-ups.
- Written procedures that sufficiently describe the control processes used for label issuing must be created; these procedures must be followed.

211.130 Packaging and labelling Operations:

- By keeping operations on other pharmacological goods physically or spatially separate, confusion and cross-contamination can be avoided.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 3, Issue 1, January 2023
Impact Factor: 7.301

- Recognizing and managing filled drug product containers that are placed aside and kept in an unlabeled state for upcoming labelling procedures in order to prevent the mislabeling of particular containers, lots, or fractions of lots. It is not necessary to identify every single container; rather, it is sufficient to know the name, strength, amount of contents, and lot or control number of each container.
- The assignment of a lot or control number that enables batch control and manufacturing history analysis to the drug product.
- Checking the suitability and accuracy of packaging and labelling materials before packing activities, and recording this check in the batch production record.

211.134 Drug product inspection:

- During finishing activities, packaged and labelled products must be inspected to ensure that the containers and packages in the lot have the proper labels.
- After finishing operations are complete, a representative sample of units must be gathered and visually checked for accurate labelling.
- The outcomes of these tests must be noted in the batch production records or the control records.

Subpart H- Holding and distribution

211.142 Warehousing Procedures:

Written guidelines for the storage of pharmaceutical items must be established and followed.
They must include:
The quality control unit's quarantine of drug items prior to release.
Keeping drug goods stored in the proper temperature, humidity, and lighting ranges to preserve their identity, strength, quality, and purity.

211.150 Distribution procedures:

Written procedures outlining the distribution of drug goods must be established and followed.
They must include:
A process wherein a drug product's oldest approved stock is supplied first. This condition may be disregarded if the departure is reasonable and only temporary.
A system that makes it easy to track each drug product's distribution to make it easier to recall it if necessary.

Subpart I – Laboratory control:

211.160 General requirements:

The appropriate organisational unit shall draught any specifications, standards, sampling plans, test procedures, or other laboratory control mechanisms required by this subpart, and the quality control unit shall review and approve any changes to such specifications, standards, sampling plans, test procedures, or other laboratory control mechanisms. At the time of performance, the requirements in this subpart must be complied with and documented. Any variation from the standards, sampling plans, test procedures, written specifications, or other laboratory control systems must be documented and justified

- The regular calibration of tools, equipment, gauges, and recording devices in accordance with a written programme that has been established and includes detailed instructions, schedules, accuracy and precision limits, and provisions for corrective action should the accuracy and/or precision limits not be met. It is forbidden to utilise instruments, equipment, gauges, and recording tools that don't adhere to specified standards.
- Determining whether or not in-process materials adhere to stated specifications and outlining the sampling and testing procedures. Such samples must be accurate and representative.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 3, Issue 1, January 2023
Impact Factor: 7.301

211.165 Testing and release or distribution:

- Prior to release, each batch of a drug product must undergo an adequate laboratory evaluation to confirm that it satisfies all of its final criteria, including the identification and potency of each active ingredient. Shortlived radiopharmaceutical batches that are subject to sterility and/or pyrogen testing may be released before the testing is finished, provided that the testing is finished as quickly as possible.
- Each batch of a drug product that must be free of objectionable microorganisms will undergo the requisite laboratory testing, if necessary.
- Drug goods that do not adhere to established norms, specifications, or other pertinent quality control requirements will be disregarded. Reprocessing is an option. Reprocessed material must adhere to all applicable standards, specifications, and other requirements prior to acceptance and use.

211.166 Stability Testing:

- Appropriate laboratory testing is required to assess whether each batch of a medicinal product that claims to be sterile and/or pyrogen-free complies with these standards. The test processes must be documented in writing and followed.
- Appropriate testing must be done on each batch of ophthalmic ointment to establish whether it complies with requirements for the absence of foreign particles and harsh or abrasive ingredients. The test processes must be documented in writing and followed. (c) Each batch of a controlled-release dosage form must undergo the necessary laboratory testing to establish whether it complies with the requirements for the rate at which each active component is released. The test processes must be documented in writing and followed.

211.173 Laboratory animals

Animals used to test parts, materials used during manufacturing, or pharmaceutical products for conformity with set specifications must be cared for and controlled in a way that ensures their suitability for the purpose for which they are used. They must be identified, and sufficient documents demonstrating their usage history must be kept.

Subpart J – Records and Reports:

211.180 General requirements:

Any production, control, or distribution record required to be kept in accordance with this part and specifically connected to a batch of a drug product shall be kept for at least a year after the batch's expiration date or, in the case of some OTC drugs lacking an expiration date because they satisfy the requirements for an exemption under 211.137, for a period of three years following the batch's distribution.

All components, drug product containers, closures, and labelling must have records kept for at least a year after the expiration date or, in the case of some OTC drugs without expiration dates because they satisfy the requirements for exemption under 211.137, for three years following distribution of the last lot of the drug product incorporating the component or utilising the container, closure, or labelling.

It is necessary to keep the written records required by this part so that the information contained therein can be used to evaluate the quality standards of each drug product at least once a year to determine whether any adjustments to the drug product's specifications, manufacturing processes, or control procedures are necessary. Such evaluations shall be conducted in accordance with written procedures that contain the following clauses:

A review of a sample of batches, whether they were accepted or rejected, and, if necessary, the documents related to the batch.

For each drug product, an analysis of complaints, recalls, returned or salvaged drug items, and investigations carried out in accordance with 211.192.

211.182 Equipment cleaning and usage :

In the individual equipment records that list the date, time, product, and lot number of each batch produced, a written record of major equipment cleaning, maintenance, use, and upkeep (aside from routine maintenance like lubrication and adjustments) shall be present. Individual equipment logs are not necessary if the equipment is only used to make one

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 3, Issue 1, January 2023
Impact Factor: 7.301

product, as long as the lots or batches of that product are manufactured in numerical order and follow the same pattern. The records of cleaning, maintenance, and use must be included in the batch record when special equipment is used.
The individuals performing and verifying the cleaning and maintenance (or, if automated equipment is used to perform the cleaning and maintenance under 211.68, just the individual verifying the cleaning and maintenance done by automated equipment) are required to date, sign, or initial the log proving that the work was completed. The log's entries must be in reverse chronological sequence.

211.186 Master production and control records:
For each drug product, including each batch size thereof, master production and control records must be created, dated, and signed (full signature, handwritten) by one person and independently verified, checked, and signed by a second person. This ensures consistency from batch to batch. A defined protocol describing how to create master production and control records must be used, and it must be followed.
Records for master production and control must include:

1. The brand, strength, and details regarding the dosing form of the substance;
2. A statement of the total weight or measure of any dosage unit, along with the name and weight or measure of each active ingredient per dosage unit or per weight or measure of the drug product;
3. A comprehensive list of components with names or codes that are specific enough to denote any unique quality characteristic;
4. An explanation of any calculated excess of component;
5. A declaration of theoretical weight or measure at pertinent processing stages;
6. A statement of theoretical yield that includes the highest and lowest percentages of theoretical yield that require further investigation in accordance with Section 211.192;
7. Detailed manufacturing and control instructions, sampling and testing procedures, specifications, special notations, and precautions to be observed. 5. A description of the drug product containers, closures, and packaging materials, including a specimen or copy of each label and all other labelling signed and dated by the person or persons responsible for approval of such labelling.

211.186 Production record review:
Before a batch is issued or distributed, the quality control unit must evaluate and approve all drug product manufacturing and control records, including those for packaging and labelling, to ensure compliance with all established, approved written processes. No matter if the batch has already been distributed or not, any unexplained discrepancy (including a theoretical yield percentage that exceeds the maximum or minimum percentages established in master production and control records) or failure of a batch or any of its components to meet any of its specifications shall be thoroughly investigated. The examination must cover additional batches of the same drug product as well as any other drugs that might have been connected to the particular failure or discrepancy.
inquiry must be documented in writing, along with the findings and next steps.

211.194 Laboratory records:
Complete data from all tests, including examinations and assays, must be included in laboratory records in order to ensure conformity with specified specifications and standards. A description of the sample received for testing with identification of source (that is, location from where sample was obtained), quantity, lot number or other distinctive code, date sample was taken, and date sample was received for testing.

- A list of all calculations made for the test, including the units of measurement, conversion factors, and equivalency factors. A statement of the results of tests and how the results compare with established standards of identity, strength, quality, and purity for the component, drug product container, closure, in process material, or drug product tested.
- The test-initials takers or signature, as well as the test's execution date or dates.
- A second person's initials or signature indicating that the original records have been checked for correctness, completeness, and adherence to accepted standards.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 3, Issue 1, January 2023
Impact Factor: 7.301

Any time an established testing procedure is modified, complete records must be kept. These records need to show why the adjustment was made and evidence that it led to outcomes that were at least as precise and dependable for the substance being tested as the original method.

211.196 Distribution record:

Distribution records must include the lot or control number of the drug product, as well as the name and strength of the product, a description of the dosage form, the name and address of the consignee, the date and quantity distributed. Distribution records for compressed medical gas products are not needed to include lot or control numbers.

Subpart K – Returned and salvaged drug product:

211.204 Returned drug products

Drug products that have been returned must be marked as such and kept. The returned drug product must be destroyed if the circumstances in which it was held, stored, or shipped before or during its return, or if the state of the drug product, its container, carton, or labelling as a result of storage or shipping raises questions about its safety, identity, strength, quality, or purity, unless examination, testing, or other investigations reveal that the drug product complies with the necessary standards of safety.

211.208 Drug product salvaging:

Drug products that have been improperly stored due to natural catastrophes, fires, accidents, or equipment failures and have been exposed to extremes in temperature, humidity, smoke, fumes, pressure, age, or radiation are not permitted to be recovered and put back on the market. Salvaging operations may only be carried out if there is proof that drug items have not been exposed to these circumstances whenever there is a doubt.

- Proof that the drug products adhere to all applicable standards of identity, strength, quality, and purity from laboratory tests and assays, including animal feeding studies when appropriate; and
- Proof that the drug products and the packaging that goes with them weren't subjected to improper storage conditions as a result of the accident from a site inspection.

REFERENCES

[1]. https://www.ecfr.gov/current/title-21/chapter-I/subchapter-C/part-211
[2]. https://www.slideshare.net/MahewashPathan/current-good-manufacturing-practicescgmpand-industrial-management
[3]. https://www.slideshare.net/ssuserfe3019/c-gmp-127323597
[4]. https://forum.daffodilvarsity.edu.bd/index.php?topic=9051.0
[5]. https://www.slideshare.net/AlakeshBharali/current-good-manufacturing-practicescgmpseminar
[6]. https://www.tuv-nord.com/in/en/blog/blog-details/article/current-good-manufacturingpractices-cgmp-in-pharmaceutical-industry/
[7]. https://www.slideshare.net/JayeshRajput7/cgmp-and-industrial-management
[8]. https://www.simplerqms.com/cgmp/
[9]. https://www.fda.gov/drugs/pharmaceutical-quality-resources/facts-about-current-goodmanufacturing-practices-cgmps